

# FLAGELLATE TRICHOMONAS HOMINIS IN THE RABBIT—ITS PATHOGENICITY\*

REPORT OF AN INSTANCE OF INFESTATION  
IN MAN, WITH NECROPSY FINDINGS

## REPORT OF CASE

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THE rôle of the intestinal parasite, *Trichomonas hominis*, in the etiology of disease in man is uncertain. As this flagellate is found in the stools of many apparently healthy persons, as well as of those complaining of a diversity of symptoms, a determination of its pathogenicity is important.

## COMMENTS ON THE LITERATURE

Infestation by this parasite has been reported from many parts of the world. Although Kofoïd,<sup>1</sup> as a result of his research in the Debarkation Hospital in New York City, believes that the eastern Mediterranean region is a source of infection, and that trichomonas is the least frequent of the common flagellates infesting man in other localities, the results of other observers tend to dispute this. In South America, Escomel<sup>2</sup> reported 152 instances observed during one year in Peru alone. Parodi<sup>3</sup> in the Argentine found more than fifty instances in the examination of 1071 persons. Wenyon and O'Connor,<sup>4</sup> examining English soldiers of the Egyptian Expeditionary Forces, reported twelve instances. In the temperate zone, Smithies<sup>5</sup> reported an incidence of two per cent infestation with *Trichomonas hominis* in 3780 persons; Kofoïd,<sup>6</sup> an incidence of 1.1 per cent in approximately 8000 individuals. The highest figure of 22 per cent is given by Sistrunk<sup>7</sup> in a series of 145 patients. In the United States, instances of infestation with this flagellate have been reported from various sections. Freund<sup>1</sup> discusses ten instances found in Detroit in 1908. Lynch<sup>8</sup> mentions instances from South Carolina and Texas. Barrow<sup>9</sup> (Los Angeles) in 1924 found ninety-seven instances of trichomonas infestation in the examination of 725 persons. Sistrunk concluded that, contrary to the popular opinion, intestinal protozoa are not confined to the South, but are often found in the stools of persons who have never resided there.

## SYMPTOMS

There is a difference of opinion regarding the symptomatology of trichomonas infestation. Some observers (Gunn<sup>10</sup> and Minchin<sup>11</sup>) express the belief that the affection is symptomless. However, weakness, lassitude, anemia, vague ab-

dominal pains, flatulence, backache, insomnia, headache, etc., are frequently mentioned. The uncertainty attending this subject is best exemplified by the opinions expressed regarding the most frequently recorded symptom—diarrhea. That its occurrence is frequent is the belief of Chandler, Smithies,<sup>12</sup> Coutant, Hinkleman, Lynch, and Escomel.<sup>13</sup> Freund<sup>1</sup> reported ten patients from Dock's clinic suffering from chronic diarrhea with trichomonas present in the stools. He defends the pathogenicity of this flagellate, and the clinical entity of the disease, trichomoniasis. Head<sup>14</sup> has found numerous instances of diarrhea associated with trichomoniasis. Sistrunk<sup>7</sup> reported thirty-two instances of *Trichomonas hominis* infestation associated with diarrhea. Kofoïd<sup>15</sup> also states that diarrhea may be caused by this organism. He believes, however, that the severe symptoms attending trichomonas infestation as reported by Alvarez (Columbia), Varezza (Argentina), and Escomel (Peru), might in reality be caused by Pentatrachomonas (an organism having one more flagella than the *Trichomonas hominis*).

There are others of the opinion that constipation is an important symptom. Bonthius<sup>10</sup> found that of seventy-four patients infested with one or more forms of intestinal protozoa, including *Trichomonas hominis*, seventy-one gave a history of constipation. Lopes,<sup>16</sup> quoting Loper, gives constipation as one of a group of symptoms in the "dyspeptic syndrome" of trichomonas infestation. Tsuchiya<sup>17</sup> found that in twenty patients carefully studied, diarrhea was not present. On the contrary, constipation was frequent.

## PATHOGENICITY

Various attempts have been made clinically and experimentally to demonstrate the pathogenicity of *Trichomonas hominis*. Having gained access to the body, the organism inhabits the large bowel. Barrow<sup>9</sup> reports that hemorrhoids, abdominal tumors, intestinal adhesions, cecal pockets, diseased appendices and gall bladders, etc., may serve as incubators. It has been claimed that the flagellate can penetrate the intestinal walls, gaining access to the blood stream. Plimmer<sup>18</sup> has isolated it from the blood of batrachians and reptiles in the London Zoölogical Gardens. Pentimalli<sup>19</sup> obtained positive blood cultures from two patients; Hinkleman,<sup>20</sup> from one.

The opinions expressed and the evidence regarding the ability of trichomonas to invade the tissues of man may be summarized as follows: Chace and Tasker<sup>21</sup> and Haughwout<sup>11</sup> state that the organism never penetrates the intestinal wall. Musgrave,<sup>22</sup> Lopes,<sup>16</sup> and others believe that the organism can aggravate intestinal lesions already present. Coutant<sup>13</sup> encountered a large number of trichomonads in the microscopic examination of mucus obtained from an erosion in the rectum of a patient with trichomonas diarrhea. Soper<sup>23</sup> reports that in some instances of infestation small linear ulcers about the diameter of a hair abound in the rectal mucosa, as revealed by the proctoscope.

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We have found one report in the literature regarding the necropsy findings in an instance of trichomonas infestation. Our survey of the literature included the abstracting of fifty-two articles in four languages dealing with *Trichomonas hominis* or closely related organisms. Death in the above instance was due to aortic insufficiency and arteriosclerosis of the kidneys. There was a diffuse pseudomembranous colitis extending from the ileocecal valve to the rectum. Actual tissue invasion was not mentioned.<sup>24</sup>

**Animal Experimentation.**—Animal experimentation has failed to elucidate the question of pathogenicity. In some instances tissue invasion appears to have occurred, but since flagellates are often indigenous to the experimental animal used, the utmost caution is necessary in the interpretation of results. Stevenson, according to Haughwout,<sup>11</sup> obtained sections from the cecum of a mouse showing definite lesions of the mucosal surface invaded by numerous trichomonads. Hadley<sup>25</sup> found the trichomonas with which he worked penetrating the intestinal walls of a turkey. Many organisms were present in the crypts of Lieberkuhn, and from there had penetrated into the muscular layers. Since the relationship of the flagellates commonly present in mice and poultry to *Trichomonas hominis* is still undetermined, these observations are of doubtful value.

Animal inoculation experiments have been tried with various members of the flagellate group. The most important are those of Hogue,<sup>26</sup> who gave a series of kittens cultures of *Trichomonas hominis* orally and by rectal instillation. Stool examinations over a period of at least a week following the inoculations failed to disclose the organism. Negative results were also obtained with two rabbits, using the rectal route of implantation. In this instance a flagellate indigenous to the rabbit was found, but careful observation of morphology demonstrated that it was not the *Trichomonas hominis*.

We have attempted to prove the pathogenicity of *Trichomonas hominis* in experimental animals, to note any characteristic pathologic changes, and to recover the organism from the affected tissues. In our experiments eleven rabbits were used for inoculation, and twenty-four for controls. The material for inoculation was obtained from the freshly passed stools of a patient with a well-marked trichomonas infestation.

The first rabbit was given, by stomach tube, the supernatant fluid from a mixture of feces and 0.85 per cent salt solution. This contained numbers of active flagellates. On the fourth day the animal's stools appeared darker than those of the control group, but since flagellates could not be found, the dose was repeated in two weeks and again in four. At autopsy four days later, no organisms could be recovered.

In the next experiment, two feedings, a week apart, of fresh *Trichomonas*-containing feces and barley were given to two rabbits after a preliminary short starvation period. One month later the organism appeared in the stools of both. At postmortem examination, two and four months respectively after the original inoculation, *Trichomonas hominis* flagellates

were isolated from material obtained from the appendix and cecum of each animal.

Two other groups, of four rabbits each, were then treated in a similar way. The first group received two doses at a six-day interval; the second, a dose on the fifth and on the ninth day after the original inoculation. The stools soon became dark or mucus-coated, but the organism was not found. At autopsy, six weeks after the beginning of the experiment, *Trichomonas hominis* flagellates were isolated from the cecal material and appendix in each instance. In the second group the rabbit flagellate was also found, confirming us in our opinion that we had been successfully differentiating between the two types of organism. Since the rabbit flagellate is often present, it might have proved a source of confusion.

Pathologic examination demonstrated the presence of numerous superficial ulcers, about one millimeter in diameter, limited entirely to the rectum, occurring twice in the experimental animals, and four times in the controls. The other organs were grossly normal. Microscopic examination of sections made from the large bowel, the appendix, and the gall bladder of each animal failed to disclose in a single instance tissue invasion by the flagellates.

#### REPORT OF CASE

We have observed one patient with a *Trichomonas hominis* infestation on whom we later made a necropsy examination.

J. G., a white boy, age two years and ten months, entered the Cottage Hospital on the service of Dr. Hilmar Koefod on November 5, 1920. He had spent a good part of his life in Texas. When sixteen months of age, he had had dysentery with blood and mucus in the stools, and a fever ranging between 101 and 103 degrees Fahrenheit for a period of two weeks. Eight months later he had fever and vomited for ten days, and since that time had been constipated and generally below par. On hospital entrance he complained of weakness, fever, and constipation. He appeared very pale and underweight. The heart was enlarged, and an apical systolic murmur was present. The spleen was palpable. The blood showed a pronounced secondary anemia, the hemoglobin being 40 per cent (Dare), and the erythrocytes numbering 1,630,000 per cubic millimeter. The leukocyte count was 3600 per cubic millimeter, of which the small lymphocytes composed 85 per cent, the neutrophilic polynuclears 8 per cent, the large lymphocytes 6 per cent, and the large mononuclears 1 per cent. The laboratory reported, on several examinations, the presence of *Trichomonas hominis* organisms in great numbers in the stools. His stay in the hospital was characterized by numerous periods of pyrexia, but he was at length discharged as improved on January 26, 1920.

He reentered the hospital on March 20, 1920. At this time he was acutely ill, pallid, and lethargic. Pus was draining from each middle ear. The tonsils were infected, and the cervical lymph glands were enlarged. No further change was noted regarding the heart. The liver was down to the iliac crest on the right. The spleen was barely palpable. A few petechiae were scattered over the abdomen. The blood picture was essentially the same as previously, except for the presence of an occasional eosinophil (one per cent) in the stained smear. The urine contained a trace of albumin, but no casts or blood cells. *Trichomonas hominis* was again found in the stools.

The clinical diagnosis was septicemia, secondary anemia, chronic tonsillitis, otitis media, and *Trichomonas hominis* infestation. Death ensued on April 7, 1920.

**Necropsy.**—The anatomic diagnoses were petechial hemorrhages in the lungs, heart, stomach, small and

large bowel, urinary bladder, kidney pelves, and peritoneum; chronic parenchymatous nephritis; generalized cardiac enlargement and left ventricular hypertrophy; infected tonsils and hyperplastic cervical lymph glands; fatty change of the liver; and passive congestion of the spleen. Culture of the heart's blood and bile was positive for *B. coli*. Cultures of the pericardial fluid remained sterile.

The serous coat of the large bowel was covered with small areas of a brownish-pink color showing neither elevation nor erosion. These lesions differed in appearance from the petechiae in other organs, consequently it was felt that they might represent another pathologic picture, perhaps due to the presence of *Trichomonas hominis*.

Microscopic examination of the gall bladder and small bowel gave no evidence of tissue invasion of these organs by the flagellate. Microscopic sections cut through the lesions in the large bowel were also made. Dr. J. V. Barrow and Dr. A. Bonthius kindly consented to study them. They could not find that a single flagellate had penetrated into the bowel wall.

**Evaluation of Findings.**—In attempting to evaluate our experimental and pathologic findings, it must be remembered that we are considering a parasite and not a bacterium. Parasites commonly cause disease, not through cell invasion and toxin formation, as do bacteria, but rather through appropriating for their own use the energy income of the host, through opening the avenues to secondary bacterial invasion and through mechanical difficulties due to their presence in the tissues. Furthermore, the parasite may well be a secondary invader in its turn. In other words, the organism may have no pathogenicity in the true sense, and the symptoms resulting from nutritional disturbance may often be explained on another basis. Conversely, Koch's postulates cannot be applied with such aptness in attempting to prove that a parasite organism is invariably the cause of a certain disease, as they can with bacteria. Under such circumstances the best we can do is to demonstrate a constancy of relationship between the presence of a parasitic organism and a typical pathologic lesion.

In considering our rabbit experiments, we can say that we did obtain an infestation of the animals by *Trichomonas hominis*. Hogue, using a similar technique, as previously noted, was unsuccessful, and is of the opinion that most workers confuse the organism with which they work with that often indigenous to the animal used. By careful attention to morphologic detail we feel that we have eliminated this source of error. Granting, then, that our animals were "infected," we might hope to find a constancy of pathologic lesion, and to demonstrate the organism in that lesion. In this we were entirely unsuccessful. There was no evidence that the organism has the ability to invade the tissues of the rabbit.

Likewise, in our patient who had a heavy infestation, although we found lesions in the large bowel differing from those in other organs, we are not justified in concluding that *Trichomonas hominis* was the cause of those lesions.

#### CONCLUSIONS

We are forced to conclude from our experiments that *Trichomonas hominis* is not patho-

genic in the rabbit. Careful study of our patient who came to necropsy warrants us in reporting the absence of any evidence of tissue invasion. Santa Barbara Cottage Hospital.

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#### DISCUSSION

HERBERT GUNN, M. D. (2000 Van Ness Avenue, San Francisco).—There has been considerable interest during the past few years in the subject of flagellate infections, and *Trichomonas hominis* has come in for its share. The authors of this paper have considered the topic from a broad standpoint and have endeavored to throw light on it from various angles. Their observations constitute a valuable contribution to our knowledge of the subject.

*Trichomonas hominis* is recognized as being of world-wide distribution. There is some discussion as to the varieties of trichomonas based on the number of flagella that are found, but classifications changing the species have not been generally accepted. There has been considerable discussion for a number of years over the pathogenicity of this parasite. All sorts of symptoms have been ascribed to it, but much that has been written on the subject proves valueless upon critical consideration.

As stated by the authors, diarrhea is the most frequently recorded symptom. This is quite natural as the parasite is never seen in the formed stool, and as no cysts are produced its presence cannot be determined unless the stool is soft or liquid. The authors also quote several observers who state that in their experience constipation is the most prominent symptom. The fact of the matter is that the finding of *Trichomonas hominis* in the stool depends very largely on the character of stools examined. If the patients present symptoms of dysentery or diarrhea, trichom-

onas will be encountered in a certain percentage. If formed stools are examined it will not be encountered at all. If a laxative is administered to persons having a normal formed stool or suffering from constipation trichomonas will be found with probably as great frequency as in the diarrhea cases. For a number of years it has been my practice to examine in every case a warm liquid stool in addition to formed stools, and the results of these examinations has led me to conclude that the incidence of trichomonas infection has very little connection with any symptoms. I have also had the opportunity of observing a number of persons who harbored trichomonas for long periods after they had received treatment for various conditions, and in none of these were there symptoms which could be definitely ascribed to this parasite.

The findings of Doctor Nuzum and his colleagues in their animal inoculations and their autopsies would tend to strengthen my belief in the nonpathogenicity of *Trichomonas hominis*.

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JOHN F. KESSEL, M. D. (Los Angeles County General Hospital, Los Angeles).—The question of the pathogenicity of the intestinal flagellates is one about which considerable speculation has occurred in the past, but one concerning which very few exact experimental data have been procured. Most opinions that have been expressed thus far have been formed merely from clinical observations without adequate experimental studies in pathology in which the bacteriologic and protozoölogic aspects of the subject have been considered.

The present study is an attempt in the right direction, but the conclusions should not be taken as final. In the light of personal experience with this same general subject, I should like to make the following suggestions. First, the rabbit is an unfortunate animal for the authors to have selected for the present study on account of its restricted diet, and because its intestinal tract is often naturally infested with other flagellates, for example, *Chilomastix cuniculi* and *Eutrichomastix*. The authors mention the possibility of confusing *Trichomonas hominis* with these flagellates, and in their minds have successfully differentiated them from *Trichomonas hominis* of man. However, they have not given adequate description of the flagellates which they encountered, nor have they presented sufficient data concerning their methods of isolation and cultures of the protozoön, nor of the isolation and feeding methods employed with their experimental animals to convince the critical reader that they were not dealing with natural flagellate infestations of the rabbit. Experiments of this type to be of value must be carried on under strict isolation conditions and the food given must be sterilized. Such precautions should be taken in order to eliminate the possibility of experimental animals acquiring natural infections during the period of the experiment.

Second: In the review of the literature the authors fail to mention Wenyon's case in which he found invasion of trichomonas into the mucosa of the human intestine. They might also have referred to recent publications by the reviewer in which, first, *Trichomonas hominis* was found in conjunction with amebae in the pus from amebic liver abscess observed in Korea, and second, a series of experimental kittens in which both diphtheritic colitis and invasion of the flagellates into the intestinal mucosa were apparent.

Third: The case history presented by the authors was so complicated by other factors that it was a most unfortunate case to use in illustrating trichomonas infestation.

In order to study this subject adequately a further series of autopsy reports on patients found to be positive for *Trichomonas hominis* should be observed. Where positive pathology is present, protozoa other than trichomonas and pathogenic bacteria and fungi must be ruled out of the picture. Only when this is

done, and when further careful experiments and clinical data are collected, will it be possible to answer the question raised by the writers.

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FRANKLIN R. NUZUM (Closing).—In answer to the questions raised by Doctor Kessel as to our experimental technique, we attempted to recognize, and eliminate so far as possible, sources of confusion and error. The animals were first carefully studied to determine the presence or absence of indigenous flagellates and their morphologic characteristics. During the experimental period the rabbits were isolated in single wire cages. They were fed steam-rolled barley and dried alfalfa, which could not have been purveyors of *Trichomonas* organisms. They drank city tap water, which, on numerous examination of centrifuged specimens, was found not to contain flagellates.

For the identification of the organism, microscopic examination of normal saline smears of fresh intestinal contents proved the most satisfactory. In such preparations *Chilomastix cuniculi* is distinguished by a whirling disk movement, and three loosely spread flagellae trailing along one side of the organism in an almost parallel plane. *Trichomonas*, on the other hand, as aptly described by Davaine, "swings like the bob of a pendulum on its shaft," and an undulatory movement is apparent outside of the contour proper of the organism. Furthermore, trichomonas has a well-marked cystostome and axostyle which serve as another point of differentiation between it and chilomastix. In addition to fresh preparations, we studied the organisms as stained by iron-alum-hemotoxin, and by nigrosin. With the latter, the four anterior flagellae of *Trichomonas hominis* readily differentiate it from the three flagellated chilomastix. The organisms were not cultured.

We feel that the results of the experimental investigation of this problem, while not conclusive, are in confirmation of the clinical impression that *Trichomonas hominis*, at least in most instances, is nonpathogenic for man. Since, to the best of our knowledge, persons do not die of trichomonas infestation, autopsy material must of necessity be complicated by other factors. Nevertheless the careful study of such material offers the best approach to the final solution of the question.

### ACNE\*

#### A STATISTICAL STUDY OF POSSIBLE RELATED CAUSES

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GILCHRIST in 1902 found the *Bacillus acne* in pure culture in many lesions of acne and present in all lesions. Since that time it has been generally recognized that the *Bacillus acne* is the primary cause of acne vulgaris; however, it has been many times stated that there are a number of predisposing factors or causes contributing to the presence of acne lesions, such as improper food, constipation, abnormal menstruation in women, endocrine disturbance, and foci of infection.

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